Understanding and Evaluating Outsourcing Alternatives

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During the past decade, the pharmaceutical and biotechnology industries greatly expanded their outsourcing of clinical drug development activities. In response to the increasing demand for its services, the outsourcing industry grew from a handful of contract research organizations (CROs) to an estimated 200 companies in the United States and more than 800 worldwide.

Equally dramatic is the diversity of outsourcing alternatives currently available. The terms *CRO*, *global CRO*, *SMO*, *AMC*, *HMO*, *PPM*, *niche provider*, and *hybrid organization* are often heard in discussions about outsourcing. What are these companies? Do the different names really indicate distinct services and capabilities? How does a sponsor choose the right type of vendor or mix of vendors for its project?

Diverse outsourcing companies offer made-to-fit choices to help sponsors streamline clinical trials.

Contract research organizations (CROs). CROs can perform a wide range of services for pharmaceutical and biotechnology companies (sponsors). Most often, sponsors contract for a CRO to perform some or all of the following services: investigator selection, site initiation, clinical monitoring, data management, statistical analysis, and report writing. Small sponsors and "virtual" companies that do not have in-house drug development capability may ask CROs to assist in a wider range of activities, including protocol development and regulatory submissions. Some larger CROs have expanded the scope of their services to include subject recruitment, clinical packaging, contract marketing, and contract sales.

Three critical factors for CRO selection are capability, compatibility, and cost (see box).[1]

Global CROs. Many large (more than 200 permanent employees) CROs and midsize (more than 50 permanent employees) CROs claim to have global capability. These providers maintain offices with permanent staffs in major cities abroad. In addition to the UK and Western Europe, some global CROs offer services in Central and Eastern Europe, Nordic countries, South Africa, and Asia. Several CROs have recently begun operations in emerging markets, such as China and Latin America.

In addition to the "three Cs" described above, sponsors should ensure that a prospective global CRO can provide both integrated global project management and integrated global data management services.

Integrated global project management means that a CRO collects "real-time" or daily project management data from its affiliates around the world. It is not sufficient for the CRO to send out a storm of faxes or e-mails to its affiliates each time the sponsor wishes to have a project update.

Integrated global data management is a CRO's ability to construct a unified database from studies conducted around the world. Problems sometimes arise when global CROs perform regional data management. For example, Asian data may be processed at a central location in Asia, European data are often processed at a central European location, and data from North American sites are usually processed at the CRO's headquarters in the United States. Using multiple data management sites poses the risk that regional data centers are following dissimilar practices and standards. The result may be that these separate databases cannot be easily merged into a single global database or merged into the sponsor's database. In order to avoid these costly delays, the sponsor must ensure that the CRO is following uniform data management practices worldwide.

Niche providers. Niche providers are usually small CROs with fewer than 50 permanent employees or medium-sized CROs that have a specific focus. Most common are contract monitoring organizations that provide investigator selection, site initiation, and site monitoring services. Other niche providers specialize in data handling or QA (quality assurance) auditing.

Niche providers usually have an intimate relationship with one or a few sponsors. This may be the result of an employee leaving a sponsor, setting up a local busi-

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Evaluating Service Providers (cont'd)

CROs

- [ ] Does the CRO have an in-house data management and biostatistics department with experience in the therapeutic area?
- [ ] Does it have sufficient resources to provide timely services?
- [ ] Do the sponsor and CRO have compatible corporate cultures?
- [ ] Are the CRO's standards and practices consistent with those of the sponsor?
- [ ] Are the CRO's proposed fees reasonable and consistent with the sponsor's budget?

SMOs

- [ ] Can the SMO provide the necessary qualified site setting (for example, private practice, managed care, or academic)?
- [ ] Is the SMO's relationship with each site exclusive (affiliated site) or nonexclusive (referred site) appropriate for the project?
- [ ] How efficient is the SMO at initiating its member sites?
- [ ] What is the average time required for study initiation at each proposed study site?
- [ ] Is documentation available to verify that each site is well qualified to undertake the study? If the SMO does not provide such documentation, the sponsor or CRO should perform its own evaluation.
- [ ] Are adequate numbers of the desired types of patients available? The sponsor should provide the SMO with a clear description of the target patient population and inclusion criteria and ask for site bias to be objective of subject availability.

AMCs

- [ ] Does it have a central office with authority to negotiate the contract and research grant, or will the sponsor or CRO have to deal with multiple bureaucratic levels and departmental turf battles?
- [ ] What is the overhead rate, and will it be applied to both direct and indirect costs?
- [ ] Can the AMC provide data on the average daily fee for IRB review?
- [ ] Will the AMC agree to the sponsor's preferred IRB?
- [ ] Does the AMC provide training for its CRCs and investigators?
- [ ] Will the central office assist in patient recruiting?
- [ ] Can the AMC provide qualified temporary personnel to maintain study continuity in the event of a CRC resignation?

HMOs

- [ ] Does the HMO have qualified investigators and staff for each study?
- [ ] Does the HMO have a centralized contracting office that can fit the contract and budget negotiations?
- [ ] What type of approval from HMO management will be required?
- [ ] How much does the HMO add to the cost of the study?
- [ ] Can a central IRB be used?
- [ ] Does the HMO provide CRC and investigator training?
- [ ] Will the study personnel (CRCs and investigators) receive additional compensation for participating in the study?
- [ ] Can the HMO project the number of patients that are likely to fit the eligibility requirements of the protocol?

PPMs

- [ ] Are the PPM's practitioners sufficiently interested in and qualified to conduct clinical studies?
- [ ] Do they have the necessary facilities and staff (for example, CRCs)?
- [ ] Will the PPM's fees significantly increase the cost of the study?
- [ ] Will the PPM facilitate negotiating the contract and budget?
- [ ] Does the PPM provide investigator and CRC training for its sites?
- [ ] Will the study personnel receive additional compensation for participating in the study?
- [ ] Can the PPM project the number of patients that are likely to fit the eligibility requirements of the protocol?

ness, and contracting services to former colleagues. Niche providers are usually highly adaptable and capable of working according to the sponsor's SOPs (standard operating procedures). In some cases, the niche provider's staff members work under the sponsor's roof and report to sponsor staff. Several agencies that provide temporary personnel have recently entered the niche provider market.

A critical area in which to evaluate potential niche providers is their ability to provide highly qualified personnel. In order to remain flexible, niche providers supplement a small permanent core staff with independent contractors. The sponsor should examine the niche provider's procedures for evaluating, selecting, and managing its contractor staff.

Site management organizations (SMOs). SMOs are companies that manage networks of clinical investigators under a central business umbrella. Their principal services include identifying investigator sites and initiating studies at these sites. Unlike CROs, SMOs do not generally provide project management, data management, statistical analysis, or regulatory services. A sponsor may contract directly with an SMO or indirectly through a CRO. Some SMOs own their study sites, while others work through affiliated sites. An in-depth discussion of the various SMO models appeared in the November 1999 issue of *Applied Clinical Trials*.[2]

The sponsor or CRO should evaluate both the SMO and the proposed study sites (see box).

Academic medical centers (AMCs). The role of academic sites in pharmaceutical industry–sponsored research has not kept pace with the growth of the outsourcing industry. Sponsors and CROs alike have complained that academic sites were too bureaucratic, too slow, and too costly. In response to these criticisms, academic medical centers were created. Several academic institutions established central offices to facilitate clinical contract and grant negotiation with sponsors and CROs. In many cases, these offices have also made headway in reducing institutional review board (IRB) review times.

Some AMCs (the Clinical Research Institute at the University of Rochester, for example) are developing training and evaluation programs for clinical research coordinators (CRCs) and for investiga-

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tors. Others, such as the Pittsburgh Clinical Research Network, are coordinating studies in large, integrated health care networks that include surrounding hospitals, clinics, and practitioners. At least one AMC, Duke Clinical Research Institute, offers a full range of CRO services: investigator selection, site initiation, clinical monitoring, data management, statistical analysis, and report writing.

Sponsors are usually attracted to a certain academic institution because of its prominence or the presence of an investigator who is a thought leader in the field. It is wise, however, to evaluate the relative ease of working with that institution (see box).

Health maintenance organizations (HMOs). HMOs may provide opportunities for conducting clinical studies. A large proportion of the population is covered by managed care, and a large percentage of practitioners belong to HMOs. Pharmacoeconomic and health outcome studies are most likely to be of interest to HMOs. A clinical study may provide an opportunity for the sponsor to demonstrate the advantages of its new product and gain favorable pricing from the HMO's formulary committee.

HMOs conduct both federally sponsored and pharmaceutical industry–sponsored studies. For example, The Center for Health Research has an affiliation with the Northwest Division of Kaiser Permanente. The center provides medical and hospital services to more than 400,000 members in northwestern Oregon and southwestern Washington and is conducting a variety of clinical studies.

A sponsor or CRO that wishes to conduct a study in an HMO setting should first answer the questions in the box.

Physician practice management companies (PPMs). PPMs were developed to organize and consolidate physician practices, thereby gaining economies of scale and more effective bargaining with suppliers. The industry grew to more than 30 single-specialty and multispecialty PPMs providing services to large numbers of practitioners and their patients. Recently, the industry suffered major losses, and several PPMs refocused their attention on conducting clinical studies for the pharmaceutical industry. Anbari, et al.,[3] have published a detailed analysis of the possible role of PPMs in pharmaceutical industry–sponsored clinical research. Because PPMs serve large numbers of community-based practitioners, they may be particularly useful for conducting Phase 4 studies and outcomes-based research. The authors point out that several major pharmaceutical companies are conducting clinical studies with the following three PPMs: MedCath (cardiology), US Oncology, and PhyMatrix (a multispecialty PPM now called Innovative Clinical Solutions, Ltd.).

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Sponsors and CROs interested in conducting studies with PPMs should evaluate the issues in the box, which are similar to those suggested for HMOs.

Hybrid CRO-SMOs. A number of CROs have begun purchasing study sites, and several SMOs now offer CRO-type services. These hybrid CRO-SMOs and hybrid SMO-CROs offer the convenience of one-stop shopping for trial management and study conduct. They present the possibility of a conflict of interest, however, if the same personnel are responsible for both overseeing and conducting the study. To minimize this risk, hybrids maintain separate reporting structures for those who conduct study management, data management, and analysis services versus those involved in the conduct of the study.

The sponsor's evaluation of a potential hybrid provider should include those areas described for both CROs and SMOs. In addition, the sponsor should ensure that no conflict of interest exists between the study management and site management staff.

The pharmaceutical sponsor has many outsourcing alternatives available to assist with clinical drug development activities. To achieve maximum benefits from outsourcing, the sponsor must first choose the most appropriate type of service or mix of services, then ensure that the provider(s) has the qualifications and resources needed to ensure success.

References

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